"PROGNOSTIC SIGNIFICANCE OF SERUM FERRITIN CONCENTRATION IN PATIENTS WITH ACUTE ISCHEMIC STROKE"

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CERTIFICATE

This is to certify that this dissertation entitled **" PROGNOSTIC SIGNIFICANCE OF SERUM FERRITIN CONCENTRATION IN PATIENTS WITH ACUTE ISCHEMIC STROKE"** is a bonafide work done by Dr. P.K. Senthil Kumar under my guidance and supervision in the department of Internal Medicine, Stanley Medical College Hospital during the period of his Post Graduate study of MD (General Medicine) From 2003 to 2006.

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INTRODUCTION

With the advent of promising therapies for Acute Ischemic stroke, comes a higher expectation for rapid recovery and good outcome. Despite these new therapies, poor outcome may still occur because ischemic stroke is a heterogenous disease in which outcome is influenced by many factors. The extent of brain Injury and the resultant outcome from inchemia is largely dictated at a physiological level by the severity and duration of the insult. Outcome is further influenced by genetic predisposition, temperature, glucose and other unknown factors.

For a Longtime serum ferritin was measured only to know the stored Iron status. Now it has been suggested that it influences the prognosis of Ischemic stroke[1] and also acts as a risk factor for Ischemic episodes by enhancing atherogenesis.[2/3]

AIM

To study the prognostic significance of serum ferritin concentration in patients with Acute Ischemic stroke.

REVIEW OF LITERATURE

Stroke or cerebrovascular accident, by definition of WHO is a rapidly developing clinical symptoms and/or signs of focal neurological deficit and at times global loss of cerebral function (coma) lasting longer than 24 hrs or leading to death with no apparent cause other than vascular origin[4].

The 24 hours threshold in the definition excludes Transient Ischaemic Attacks (TIA).

Stroke includes a number of syndromes with differing etiologies, epidemiology, prognosis and treatment. These are listed in the WHO's international classification of diseases (1975).

a. Sub arachnoid haemorrhage – 1-2%
b. Cerebral haemorrhage – 10%
c. Cerebral thrombosis or embolism – 85%
d. Occlusion of precerebral arteries.
e. Transient cerebral ischaemia of more than 24 hours
f. Ill defined cardiovascular disease (i.e, underlying pathology in brain is not determined.

Stroke is a world wide health problem making an important contribution to morbidity, mortality and disability in developed as well as in developing countries.

Cerebral thrombosis is usually the most frequent form of stroke encountered in clinical studies, though there are substantial differences in frequency from place to place. Subarachnoid haemorrhage and cerebral embolism come next, in both mortality or morbidity.

Cerebral Ischaemia is caused by a reduction in blood flow that lasts for a several seconds to few minutes. Neurologic symptoms are manifest within 10 sec. because neurons lack glycogen and suffer rapid energy failure. This cerebral Ischaemia or infarction is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart.

The causes of Ischaemia-infarction are:

Ischaemic Stroke

a. Thrombotic – 25%

i. Lacunar stroke - 20-25%

ii. Large vessel - 1-5%

b. Embolic – 75%

i. Cardioembolic - 20%

ii. Artery-Artery - 15%

iii. Cryptogenic - 30%

iv. Other - 10%

Pathophysiology of Cerebral Ischaemia

The brain is an obligatory aerobe. It derives its energy from the oxidative metabolism of glucose. There are only negligible stores of glucose in the brain. So when the cerebral blood flow falls and the brain becomes ischaemic a series of function and neurophysiological changes, which are dependent on the oxidative metabolism of glucose to provide energy in the form of ATP occur at various thresholds of flow[5].

The normal cerebral blood flow (CBF) in man is 50ml/100 gms of brain/min. Using Positron Emission Tomography, the cerebral energy metabolism is measured as cerebral metabolic rate of oxygen ($CMRO_2$) and of glucose (CMR glu). It has also been studied that the oxygen extraction fraction (OEF) remains the same through out the brain[6]. Therefore in resting normal human brain, the CBF is a reliable reflection of $CMRO_2$.

In ischaemia when CBF falls below about 20ml/100g/min[7], the oxygen extraction fraction becomes maximal and the $CMRO_2$ begins to fall. Infact a high OEF is only seen early after acute ischaemic stroke, in the first day or so.

If flow is restored, functional recovery is still possible. At this stage, lactate production increases due to ineffective anaerobic metabolism of glucose. The pH falls and ATP synthesis is impaired. As flow falls further, energy-dependent functions of the cell membranes become progressively affected. Water, Sodium and Chloride enter the cells. Calcium also enters and Potassium (K^+) leaks out[8]. Cellular transport mechanisms and neurotransmitter systems fail. Certain potentially neurotoxic transmitter are released such as L-glutamate. The oxygen radicals and lipid peroxides are formed, So damaging cells further[9]. Neurons start releasing PAF, (Platelet Activating Factor) which may be neurotoxic.

When the blood flow falls further less than 10ml/100gm/min, infarction occurs and even if flow is restored function does not recover. At this stage, the $CMRO_2$ and CMF is low and OEF will be normal indicating pure metabolic depression. Sometimes the OEF may be low indicating the CBF is in excess of requirements for the low metabolic demands of the infarcted tissue. It is called luxury perfusion. In absolute luxury perfusion, CBF is increased which is termed as hyperfusion.

The consequences of the fall in CBF depend not just on the depth of ischaemia, but also on its duration. In focal ischaemia, flow is almost never reduced to zero because of the collateral blood supply, which is therefore, a further factor in determining the metabolic consequences. The local CBF may also be influenced by the development of cerebral edema and raised intracranial pressure. Acid metabolites and the increasing extracellular potassium concentrations cause vasodilation. Vasoconstrictor prostaglandins are released from aggregating platelets and damaged cell membranes.

Blood viscosity and aggregation of formed elements slow the microcirculation and eventually thrombosis sets in. The metabolic consequences of ischaemia may be exacerbated in the presence of high prevailing glucose concentration. But the worst outcome may be related to the hyperglycaemia of stress response and reflect the severity of initial stroke. When the lactate levels are increased, seizures may occur.

Systemic hypoxia (as a consequence of pneumonia etc) and dehydration by, increasing the hematocrit and blood viscosity are further exacerbating factors.

Damaged brain may also have impaired responses to $PACO_2$ and PaO_2 as well as impaired autoregulation and perfusion reserve. This makes the brain very sensitive to any further insults such as systemic hypoxia, hypotension and raised intracranial pressure.

Free Radical Damage

Three major molecular events in brain damage from cerebrovascular occlusion are at present the focus of interest: calcium overload, excessive acidosis, and enhanced production of free radicals. Free radicals are generated in increased amounts under ischemic conditions and react with and damage proteins, nucleic acids, and membrane lipids, disrupting cellular integrity. This oxygen radical activity is especially intense during reperfusion after sustained ischemia. The generation of radical hydroxyl, the most toxic and reactive of free radicals, is catalyzed by ferrous iron released hydroxyl, the most toxic and reactive of free radicals, is catalyzed by ferrous iron released from intracellular stores during ischemia; thus the sensitivity of neurons to oxidative stress depends on the availability of iron in the ischemic focus. Iron is released from large transport proteins, particularly from ferritin, which accounts for one third to three quarters of brain iron. In the absence of inflammation, cancer, and infectious diseases, the serum concentration of ferritin is thought to be directly proportional to tissue iron stores and can be used to assess their size.

Increased body iron stores may also cause progressing stroke by enhancing the release of glutamate, a neurotransmitter in the brain. Brain cells release glutamate as a result of stroke and glutamate triggers biochemical reactions that lead to brain cell death, including the production of free radicals in brain tissue.

Risk factors for cerebral infarction

1. Unmodifiable risk factors.
2. Major modifiable risk factors.
3. Questionable rare or weak modifiable risk factors.
4. Risk factors predominant in the young.

Risk factors for cerebral infarction

Unmodifiable risk factors	**Questionable, rare or weak modifiable risk factors**	**Risk factors predominant in the young**
Age	AIDS	Mitral valve leaflet prolapse
Sex	Alcohol	Sickle cell disease and other hemoglobinopathies
Race	Fibrinogen and platelets	Migraine
Family history	Lipids	Cocaine abuse
Previous stroke	Exercise	Obstructive sleep apnea
	Hematrocrit	Intercurrent infection

Major modifiable risk factors		
Atrial fibrillation	Water supply	Patent foramen ovale
Hypertension	Anticardiolipin antibodies	Atrial septal aneurysm
Isolated systolic hypertension	Oral contraceptives	System lupus erythematosus
Myocardial infarction	Pregnancy	
Other heart disease	Homocystinuria	
Diabetes mellitus	Diet	
Transient ischaemic attacks	Socioeconomic status	
Smoking	Season Claudication	

A. Unmodifiable Risk Factors

a. Age

Age is the single most powerful risk factor for cerebral infarction. Since the increase with age is exponential, doubling or tripling with every decade after the fifth[10].

b. Sex

Mortality rates for men are 23% to 115% higher than for women in all countries[11].

c. Race

There is generally a higher incidence of all stroke types and cerebral infarction in blacks[12].

d. Previous stroke

The recurrence rate of cerebral infarction is 10-30%. The first 6 months is the period of highest risk[13]. Hypertension, Diabetes and Smoking increase the risk, while an infarction of undetermined cause is associated with a diminished risk.

2. Modifiable risk factors

a. Atrial Fibrillation

Atrial fibrillation causes 20% of all infarcts[14] and is associated with a relative risk of death from stroke of 12.25[15]. Silent infarcts are found in 20% more of the population with atrial fibrillation and this is exacerbated by increasing age and left atrial diameter[16].

b. Hypertension

After age, hypertension is the most powerful risk factor for cerebral infarction. Both systolic and diastolic pressures are important. Sex differences are not prominent in

analyses of the effects of hypertension on stroke. Prolonged treatment of diastolic BP to produce a fall of 6mm Hg decrease the stroke risk by 40% and the benefits occur within 3 years[17].

c. Myocardial infarction

Cerebral infarction occurs in between 1% and 1.25% of cases within 1 year after myocardial infarction[18]. Transmural infarcts pose a greater risk than suberndocardial infarcts. A history of myocardial infarction is also a risk factor for cerebral infarction[19].

d. Other heart disease

Cardiac disease in general, doubles the risk of stroke. While left ventricular hypertrophy quadruples it, independent of hypertension[20]. Cardiac failure, coronary heart disease and angina increases the risk of cerebral infarction.

e. Diabetes Mellitus

Though variable, the evidence now support diabetes as a risk factor for stroke[21]. Impaired glucose tolerance may be a risk factor and an elevated glycosylated hemoglobin may be found in upto 42% patients with cerebral infarcts not previously known to have diabetes.

f. Transient Ishchaemic Attacks

The incidence of stroke increases after TIA. The relative risk of stroke after TIA is 13.4 in the first 12 months and 7 over first 7 years[22].

g. Smoking

Smoking is one of the most important risk factors. There is a dose response relationship, the risk doubling in the heaviest of smokers[23]. In the Framingham study, cessation of smoking removed the additional risk of stroke within 2 years.

h. Alcohol

The effect of alcohol on cerebral infarction has two aspects. These are sudden heavy (binge) drinking and chronic consumption. There is evidence for an association between sudden heavy drinking and the onset of cerebral infarction in young adults[24]. Chronic light alcohol intake is associated with a decreased risk of stroke[23]. Chronic heavy consumption 180 – 400 g/wk is associated with an increased risk.

i. Lipids

Total cholesterol has a weak association with cerebral infarction. Framingham study suggest a weak correlation between cholesterol and triglycerides and the risk of atherothrombotic brain infarction.

j. Exercise

Lack of exercise may increase the risk of stroke in women[25].

Minor factors

Soft water has been associated with an increased risk (7%) of death from stroke according to death certificates.

Anti Cardiolipin antibodies are associated with an increased risk for cerebral infarction.

Homocystinuria is a recognised high risk factor for stroke.

Acquired ImSmuno Deficieny Syndrome (AIDS) is a risk factor for infarction. The precise mechanism is unknown, but an associated CNS infection typically with cryptococcus species, tuberculosis or varicella zoster is implicated in half of the cases.

Pathophysiology of ischaemic stroke subtypes

Cerebral infarction is not a single disease and the differentiation of several clinical, pathophysiologic and etiologic subtypes may be critical for adequate management of patients.

The most common mechanisms of ischaemic stroke is embolic, either from an atheromatosus arterial lesion (artery to artery thromboembolism) or from the heart (cardio embolism). Less commonly, in situ occlusion of an extra cranial or a cerebral artery may be incriminated in the absence of embolism.

- First, when the occluded artery is a small perforating branch without collateral supply i.e.(lacunar infarct)[26].

- Second, when large-artery occlusion may produce hemodynamic failure in the corresponding territory because of lack of functioning anastomoses (Hemodynamic infarction).

- Finally, abnormalities of the blood, itself may lead to ischaemic stroke (eg) coagulation disorders hyperviscosity, anaemia, leukemia and related disorders.

Intracranial atherosclerosis play a major role in Asians and to a lesser extent in blacks. In whites, extracranial atherosclerosis causes artery to artery embolism. However this distinction is valid mainly for anterior circulation. While recent studies have shown that intracranial vertebral artery or basilar artery atherosclerosis is also an important cause of posterior circulation infarcts[27].

MIDDLE CEREBRAL ARTERY – SUPERFICIAL TERRITORY INFARCTS

Superficial branches of the middle cerebral artery (MCA) originate distal to the origin of lenticulostriate arteries. As they course in the subarachnoid space, they are called pial branches. They supply the cortical, subcortical territory of the MCA after the MCA trunk divide in to two (upper and lower) or three (upper, middle and lower) divisions which in their turn divide into several branches.

MCA pial territory infarcts may be partial when only a distal branch is occluded, or they may be rather large when the occlusion is more proximal at the level of the MCA

bifurcation or trifurcation and the collateral system is not adequate. Because one characteristic of the pial artery network is to have extensive anastomoses, multiple distal emboli are necessary.

Actually, atleast, half of the patients with MCA pial territory infarct may show angiographic evidence for distal occlusion, suggesting embolism and most of the angiography normal cases may be due to delayed performance of angiography because these occlusions tend to disappear early.

The presumed cause of embolism is large-artery disease (>50%) internal carotid artery (ICA) or MCA stenosis or occlusion in one third of the patients and cardiac disease in one quarter of the patients[28]. Interestingly, potential cardiac sources of embolism are particularly common with infarcts in the territory of the upper division.

Because most of the frontal, temporal and parietal lobes are supplied by the MCA pial branches, the neurologic picture may be variable according to the location of the infarct.

INFARCTS IN THE TERRITORY OF THE DEEP PERFORATORS FROM THE CAROTID SYSTEM

In contrast to the pial artery network, the deep perforators from the distal ICA or the MCA trunk are terminal branches that perforate the basal part of the cerebral

hemispheres. For that reason, occlusion of one or several perforators is always associated with an infarct usually small in the corresponding territory. These small deep infarcts are often called ‘Lacunar’, but it should be remembered that lacunar may be caused by non ischaemic processes such as small haemorrhage or non ischaemic dilatation of periarteriolar space.

It is widely accepted that lacunar infarcts are usually due to in situ occlusion of the corresponding small perforator by a micro atheromatous or lipohyalinotic process associated with chronic arterial hypertension. This assumption appears correct for very small lacunar infarcts (<0.3-0.5 cm) associated with occlusion of one single perforator but these infarcts are usually asymptomatic[26]. Although small artery disease probably remains a leading etiology, in larger (0.5-1.5 cm or larger) and symptomatic small deep infarcts, other potential causes may have a potential cardiac source of embolism or large artery disease (>50%) ICA stenosis or occlusion, often in the absence of concomitant hypertension[29].

Embolism to the MCA trunk is a particularly common cause of complete lenticulostriate territory infarction (known as large striata capsular infarcts or extended infarcts of the lentiform nucleus), by occluding the lenticulostriate arteries at their origin while collateral circulation explains sparing of the superficial pial territory[30].

While it is unclear if large-artery or cardiac disease is just co-incidental in many patients with small deep infarct, it is likely that atherosclerosis of the MCA trunks (or of the basilar artery for small paramedian infarcts in the brain stem), which can occlude the origin of deep perforators has largely been overlooked as a potential etiology of small deep infarcts. Moreover, hypertension does not seem to be the only factor associated with small-artery disease leading to lacunar infarction, Diabetes mellitus should also be considered.

Clinical manifestations are largely dependant on the size of infarct. The large infarcts may produce dysfunction not markedly different from superficial MCA territory infarcts[31]. Smaller infarcts have often been linked to isolated contralateral motor or sensory disturbances (lacunar syndrome).

The classic lacunar syndrome are:

1. Pure motor hemiparesis from an infarct in the posterior limb of the internal capsule or basis pontis, the face, arm and leg are almost always involved.

2. Pure sensory stroke – from an infarct in the ventro lateral thalamus.

3. Ataxic hemiparesis – from an infarct in the base of the points.

4. Dysathria and a clumsy hand or arm due to infarction in the base of the pons or in the genu of the internal capsule.

5. Pure motor hemiparesis with motor or Brocas aphasia due to thrombotic occlusion of a lenticulostriate branch supplying the genu and anterior limb of the internal capsule and adjacent white matter of the corona radiata.

The artery of Heubner from the anterio cerebral artery (ACA) and the anterior choroidal artery from the carotid siphon are not only perforators, because they also supply cortical territories. Thus, their system of supply can be compared with that of the MCA and their etiologic spectrum of infarction is similar[32].

ANTERIOR CEREBRAL ARTERY INFARCTS

Although the ACA originated from the carotid system at the same level as the MCA, ACA territory infarcts are between 20-30 times less common than MCA territory infarcts. However, etiologic patterns do not differ between MCA and ACA territory infarcts.

Infarcts in the territory of Heubner's artery or in the territory of the anterior striate branches are usually discussed together with lenticulostriate infarcts in general.

In ACA, pial territory infarcts, the association of crural hemiparesis, mutism at onset, transcortical motor aphasia, frontal tasks impairment, mood disturbance, incontinence, grasp reflex and unilateral left apraxia may help to localize the infarct before Computer Tomography or Magnetic Resonance Imaging, but proportional (arm-

leg-arm) hemiparesis or hemisensory defect, hemineglect or confusional state may be misleading. Simultaneous bilateral ACA territory infarction may occur in relation to a common origin of both ACAs. Akinetic mutism with incontinence and bilateral grasp reflex is suggestive or this type of infarct, which is uncommon (<10%)

BORDER ZONE CEREBRAL INFARCTS

Infarction may develop at the level of the collateral border zone between two main pial arterial territories. Those extra territorial infarcts are commonly called watershed or distal field infarcts. They usually occur between the ACA and MCA territories anterior water shed infarcts or between the MCA and posterior cerebral artery (PCA) territories – posterior water shed infarcts.

In anterior water shed infarcts, hemiparesis, predominating in the lower limb, with transcortical motor aphasia when lesion is on the left, is the most common neurologic finding when the infarct predominates in the subcortical white matter, mimicking ACA territory infarction. However, when the infarct is limited to the cortex, proximal brachial hemiparesis is present because junction of the ACA and MCA territories is at the level of the arm-shoulder representation on the motor strip, thus in bilateral anterior watershed cortical infarcts, a picture bi-brachial paralysis (man-in-the-barrel) may occur.

Posterior watershed infarcts yield a neurologic picture that is similar to that of posterior MCA pial territory infarcts except for a more common occurrence of transcortial sensory aphasia.

Bilateral watershed infarcts often have a symmetrical pattern. They usually develop in relation to episodes of severe hypotension, cardio circulatory distress, prolonged hypoxemia or bilateral severe carotid disease[33]. Ventero lateral watershed infarcts are also associated with some degree of hemodynamic failure (hypotension, bradycardia, high hematocrit level) in patients with ipsilateral carotid occlusion or tight stenoses. They are good examples of hemodynamic infarcts, though microemboli may account for border zone infarcts.

An infarction between the deep and superficial (pial) territories of the MCA is uncommon. It is sometimes called a sub cortical watershed or internal watershed infarct[34]. However the term watershed may be inappropriate because it implies a border zone between two pial territoreis at the level of their collateral network. Infact, no such collaterals exist between and the pial branches of the MCA system. For this season, the term subcortical junctional or border zone infarcts seems more appropriate[35]. Hemiparesis with or without hemisensory disturbance is the most common neurologic disturbance.

POSTERIOR CEREBRAL ARTERY SUPERFICIAL TERRITORY INFARCTS

The superficial (pial) branches of the PCA include the hippcampal, medial temporo – occipital, splenial, internal occipital and calcarine branches. The posterior choroidal branches have an internal temporal pial network, but they are usually considered with the deep branches of the thalamus. Infarcts limited to the territory of just one branch of the PCA are the most common type of PCA pial territory infarction (uniterritorial), often involving the calcarine artery territory. Isolated mediotemporal involvement is rare. The most common biterritorial infarct combines calcarine and internal occipital arteries territory involvement.

The neurologic manifestations are dominated by visual symptoms, which may be simple (hemianopia) or complex (alexia, achromatopsia, agnosia, visual memory impairment).

In pathologic series, PCA infarction is often due to compression by edema during temporal lobe herniation. In a clinical setting the etiology is usually embolic, mainly from the heart, vertebro basilar atherosclerosis.

THALAMIC INFARCTS

The arterial supply to thalamus may be divided into four main groups.

1. The paramedian or thalomo perforate branches from the P_1 segment of teh PCA. They also supply the most rostral paramedian part of the mid brain (vertical gaze dysfunction, disturbed consciousness, amnesia and other neuro behavioural dysfunction).

2. The infero lateral or thalamo geniculate branches from the P_2 segment of the PCA. These arteries supply the ventero lateral mass of the thalamus (hemisensory disturbances, hemi ataxia).

3. The posterior chorodial arteries (one lateral and one medial group) from the P_2 segment of PCA. These supply posterior part of thalamus and also contribute to supply of the geniculate bodies and medial temporal lobe together with the anterior chorodial artery (mainly visual hemifield disturbances such as horizontal sectoranopia).

4. The tubero thalamic or polar branches originate from posterior communicating artery so that they are laterally at the interfall between the carotid and vertebro basilar systems. They supply the anterolateral part of the thalamus (Neuropsychologic dysfunction such as dysphasia, amnesia, neglect).nicating artery so that they are laterally at the interfall between the carotid and vertebro basilar systems. They supply the anterolateral part of the thalamus (Neuropsychologic dysfunction such as dysphasia, amnesia, neglect).

The etiology of thalamic infarct is varied. Small vessel disease associated with hypertension or diabetes accounts for not more than one third of the cases, while cardio embolism and artery-to-artery embolism accounts for atleast 25% to 30%. Other causes such as arteritis, migraine and so on may also be responsible. Usually simultaneous occlusion of several perforators (from embolism) may be necessary to lead to infarct.

BRAIN STEM INFARCTS

Mid brain, pontine and medullary infarcts usually develop in characteristic territories in relation to a stereotyped blood supply system which includes (from medial to lateral side) paramedian perforating branches and short circumferential arteries directly from the basilar artery and large cirumferential arteries, which are infact the three cerebellar arteries:

1. The Superior Cerebellar Artery (SCA)

2. Anterior Inferior Cerebellar Artery (AICA) and

3. Posterior Inferior Cerebellar Artery (PICA) and supply the dorsal brain stem as well as their cerebellar territory.

Most of the clinically relevant brain stem infarcts involve the paramedian and lateral (short circumferential branches) territories. Thus, they may be associated with small-vessel disease (lacunar infarction) but also with basilar artery (for the pons and mid

brain) or vertebral artery (for the medulla) disease that obstructs the mouth of these small arteries (branch disease). Large embolism, which may stop more proximally in the basilar artery, lead to large infarcts not limited to the brain stem. The neurologic manipulations causes by brain stem infarcts are multiple.

CEREBELLAR INFARCTS

1. PICA Territory Infarcts

PICA territory infarcts are the most common type of symptomatic cerebellar infarcts. Most cases seem related to atheromatous occlusion of the vertebral artery, less commonly the PICA itself.

2. AICA Territory Infarcts

AICA territory infarcts are the less common type of cerebellar infarcts. Infarcts in the lateral part of the lower pons is usual in association with cerebellar involvement[36]. Contrary to PICA and SCA territory infarcts, cardioembolism seems to be an uncommon cause. Atherosclerosis plays a major role.

SCA Territory Infarcts

In SCA territory infarcts, clinically relevant brain stem (mid brain) involvement is less common than in AICA territory infarcts, where cardio embolism is a classic cause.

Other Cerebellar Infarcts

Large cerebellar infarcts are usually MCA territory infarcts in patients with AICA aplasia. They are typically responsible for a rapid deterioration, tonsillar herniation and death in the absence of surgical intervention.

Watershed cerebellar infarcts may occur at the border zone between PICA, SCA and AICA territories. Their clinical diagnosis is controversial since the overlap of the cerebellar arteries may be particularly variable.

Small cerebellar infarcts have been reported in presumed cerebellar border zones, but also within the main cerebellar territories.

Venous cerebellar infarcts are usually large with a pseudo tumoural course.

INVESTIGATIONS

COMPUTER TOMOGRAPHY (CT)

The role of Computer Tomography in the diagnosis of cerebral infarction is well established. CT can distinguish between an ischaemic bland-non haemorrhagic stroke, haemorrhagic infarction and primary intracerebral haemorrhage[37].

In the clinical setting of a transient ischaemic attacks (TIA) the CT scan is usually normal, however, the detection of white matter or capsular hypodensity (chronic ischaemic change) establishes the presence of underlying vascular disease.

The classic neuropathologic process that occur during the evolution of an infarction is well reflected by the CT scan. The radiologic imaging characteristics are divided in to four stages and are dependant on the time from the onset of ictus. These stages are divided into

1.	Hyperacute	less than 24 hrs
2.	Acute	24 hrs – 7 days
3.	Subacute	8-21 days
4.	Chronic	more than 21 days

MAGNETIC RESONANCE IMAGING (MRI)

Image contrast with magnetic resonance imaging is dependant on three tissue variables. T_1 – Relaxation time, T_2 – Relaxation time and Proton density.

Ischaemia one hour after the event can be detected by MR imaging. MRI reliably documents the extent and location of infarction in all area of the brain, including the posterior fossa and cortical surface. Diffusion weighted imaging is more sensitive for early brain infarction. Magnetic Resonance angiography is highly sensitive for extracranial internal carotid plaque as well as intracranial stenosis of large vessels. MRI proves superior information compared with CT in nearly every case of stroke.

CEREBRAL ANGIOGRAPHY

Conventional X-Ray cerebral angiography is the “gold standard” for identifying and quantifying atherosclerotic stenoses of the cerebral arteries and other pathologies. Recent studies have documented that intra arterial delivery of thrombolytic agents to patients with acute MCA infarct can effectively recanalize vessels and improve clinical outcomes.

PREDICTION OF STROKE OUTCOME

The outcome of stroke is influenced by many factors. Among them, some of the most important are demographic factors such as age, sex, etc, risk factors, clinical examination findings, laboratory tests and imaging. These factors provide important insight regarding outcome.

1. DEMOGRAPHIC FACTORS

a. Age

It is one of the major factors, which can negatively influence the outcome. Poor outcome in old age is due to increased frequency of secondary complications such as pneumonia, bed sores etc.

b. Gender

Previous stroke and atrial fibrillation causes more disability and associated with increased mortality.

3. CLINICAL FINDINGS

a. Level of Consciousness and Gaze Deviation

A decrease in the level of consciousness and presence of gaze deviation indicates poor outcome.

b. Blood Pressure

Systemic hypotension can cause a fall in cerebral blood flow which may cause a decreased blood flow to the infarcted area.

A rise in BP may have long term adverse effects on the blood brain barrier. Under severe hypertension the infarcted area can go for haemorrhagic transformation.

Temperature

A two fold increase in the relative risk for poor outcome in stroke is seen with every 1^{o} C rise of temperature. This effect may be due to exctitoxic neurotransmitters.

COMPLICATIONS

The most important local complicaiton of cerebral infarction is the development of cerebral oedema, which impairs, possibly only temporarily, local blood flow and neuronal function over a wider area than just the infarct and, if extensive, causes transtentorial herniation. There are a number of general complications of acute paralysis which include bronchopneumonia, particularly if consciousness or swallowing are impaired; venous thromboembolism; pressure sores and septicaemia; urinary infection, particularly if catheterization is necessary, and eventually uraemia; contractures in spastic limbs; frozen shoulder; cardiac rhythm disturbances; and mood disorder (Table). Death in the first week is almost always due to the infarct itself and the effects of cerebral oedema, but later it is more often due to one of the general complications, particularly pneumonia.

Table

General complications of stroke

Respiratory	Pneumonia Inhalation Pulmonary embolism
Cardiovascular	Myocardial infarction Cardiac failure Cardiac arrhythmia Neurogenic pulmonary oedema
Infections	Pneumonia Urinary Skin Septicaemia
Metabolic	Vomiting Dehydration Electrolyte imbalance Hyperglycaemia Renal Failure
Mechanical	Spasticity Contractures

Mechanical	Malalignment/subluxation/frozen shoulder Falls and fractures Osteoporosis Ankle swelling Peripheral nerve pressure palsies
Others	Pressure sores Depression, anxiety, apathy Epileptic seizures Deep venous thrombosis Acute gastric ulceration Incontinence of urine/faeces

Course and Prognosis

When the patient is seen early in the course of cerebral thrombosis, it is difficult to give an accurate prognosis. No rules have yet been formulated that allow one to predict the course with confidence. A mild paralysis today may become a disastrous hemiplegia tomorrow, or the patient's condition may worsen only temporarily for a day or two. In basilar artery occlusion, dizziness and dysphagia may progress in a few days to total paralysis and deep coma. The course of cerebral thrombosis is so often progressive that a cautious attitude on the part of the physician is justified in what first appears to be a mild stroke.

As indicated above, progression of the stroke is due most often to increasing stenosis of the involved artery by mural thrombus. In some instances, extension of the thrombus along the vessel may block side branches and hinder anastomotic flow. In the basilar artery, thrombus may gradually build up along its entire length. In the carotid system, thrombus at times propagates distally from the site of origin in the neck to the supraclinoid portion and possibly into the anterior cerebral artery, preventing collateral flow from the opposite side. In middle cerebral occlusion, retrograde thrombosis may extend to the mouth of the anterior cerebral, perhaps secondarily infarcting the territory of the vessel. Embolic particles from the site of an incompletely thrombosed artery (artery-to-artery embolism) may precipitate an abrupt change. Sometimes a completely thrombosed artery or an artery whose lumen is narrowed by a dissecting aneurysm can be the source of the embolus to more distal branches after a period of several days.

Several other circumstances influence the immediate prognosis in cerebral thrombosis. In the case of very large infarcts, swelling of the infarcted tissue may occur, followed by displacement of central structures, tentorial herniation, and each of the patient after several days. Smaller infarcts of the inferior surface of the cerebellum may cause a fatal foramen magnum herniation. Milder degrees of swelling and increased intracranial pressure may cause apparent progression for 2 to 3 days but do not prove fatal. In extensive basilar infarction associated with deep coma, the mortality rate approaches 40 percent. If coma or stupor is present from the beginning, survival is largely determined by the success in keeping the airway clear, controlling brain edema,

preventing aspiration pneumonia, and maintaining fluid and electrolyte balance. Respiratory and urinary infections are constant dangers; once they begin, there is usually a rapid decline in the patient's condition as body temperature rises. With smaller thrombotic infarcts, the mortality is 3 to 6 percent.

Characteristically, the paralyzed muscles are flaccid in the first days or weeks following a stroke; the tendon reflexes are usually unchanged but may be slightly increased or decreased. Gradually spasticity develops, and the tendon reflexes become brisker. The arm tends to assume a flexed adducted posture, and the leg an extended one. Function is rarely if ever restored after the slow evolution of spasticity. Conversely, the early development of spasticity in the arm or the early appearance of a grasp reflex may presage a favourable outcome. In some patients with extensive temporoparietal lesions, the hemiplegia remains flaccid. If the internal capsule is not interrupted completely in a stroke that involves the lenticular nucleus or thalamus, the paralysis may give way to hemichoreoathetosis, hemitremor, or hemiataxia, depending upon the particularly anatomy of the lesion. Bowel and bladder control usually returns; sphincteric disorders persist in only a few cases. Often the hemiplegic limbs are at first tender and ache on manipulation. Nevertheless, physiotheraphy should be initiated early in order to prevent psuedocontracture of muscles and periarthritis at the shoulder, elbow, wrist, knuckles, knee, and ankle. These are frequent complications and often and source or pain and added disability, particularly in relation to the shoulder. Occasionally, atrophy of bone and pain in the band may accompany the shoulder pain (shoulder-hand syndrome). An annoying

feeling of dizziness and unsteadiness often persists after damage to the vestibular system in brainstem infarcts.

Recurrent convulsive (epileptic) seizures are relatively uncommon sequelae of thrombotic strokes in comparison to embolic cortical infarcts, which are followed by recurrent focal or generalized seizures in more than 20 percent of patients.

Many patients complain of fatigability and are depressed, possibly more so after strokes that involves the left frontal lobe (Starkstein et al.). The explanation of these symptoms is uncertain; some are expressions of a reactive depression. Only a few patients develops serious behaviour problems or are psychotic after a stroke, but paranoid trends, ill temper, stubbornness, and peevishness are common.

Finally, in regard to prognosis, it must be mentioned that having had one thrombotic stroke, the patient is at risk in the ensuing months and years of having a stroke at the same or another site, especially if there is hypertension or diabetes mellitus. When multiple infarcts occur over a period of months or years, a dementia may develop, in addition to focal cerebral deficits. As a group these cases are referred to as multi-infarct dementia. In some of these cases, the major lesions involve the white matter with relative sparing of the cortex and basal ganglia. This type of lesion is often referred to as Binswanger’s subcortical encephalopathy, which is equated with multiple white matter infarcts and lacunes. The part of the white matter that are destroyed have been shown to lie in the border zones between the penetrating cortical and basal ganglionic arteries.

MATERIALS AND METHODS

Setting	: -	Medical wards Government Stanley Hospital
Study Design	:-	Single center observational prospective hospital based study.
Period of Study	:-	February 2005 to February 2006.

Government Stanley Hospital is a tertiary care institute and referral center for patients from all over south India. All stroke patients admitted within the above period and who satisfied the set criteria were included.

INCLUSION CRITERIA

Patients with stroke as defined by WHO criteria.

Rapidly developing clinical signs of focal or global (coma) neurological deficit lasting more than 24 hrs or leading to death with no apparent cause other than Vascular origin.

All patients who presented within 48 hrs of onset of stroke and who gave informed consent to participate in the study were included

EXCLUSION CRITERIA

Patients with sub arachnoid haemorrhage, extra dural haemorrhage, sub dural haemorrhage and intra cerebral haemorrhage were excluded by CT scan brain.

As ferritin is an Acute phase reactant samples are taken with in 48 hrs of onset[38] and patients with high ESR / CRP were excluded.

Diagnostic procedures, treatment and all stages of rehabilitation took place according to prevailing norms and protocols. The treating physicians advice was exercised if and when found necessary.

Serum Ferrtin was measured when the patient was admitted and was correlated with functional recovery of the patients after 4 weeks. Patients were reviewed 4 weeks after onset of stroke and were stratified using glasgow outcome scale.(GOS)

GOS was used to assess the functional outcome and residual neurological deficits.

Glasgow outcome scale

1. Indicates death
2. Vegetative state (patient is unable to interact with environment).
3. Severe disability (patient is unable to live independently but can follow commands).
4. Moderate disability (patient is capable of living independently but unable to return to work)
5. Mild or no disability (patient can return to work)

Scale 4/5- favourable outcome

Scale 1/2/3-unfavourable outcome

PRINCIPLE OF THE ASSAY

UBI MAGIWEL FERRITIN Quantitative test system is a solid phase enzyme-linked immunosorbent assay (ELISA). The wells coated with specific anti FERRITIN antibodies are incubated with samples (standards and unknown samples) and another anti-ferritin antibodies conjugated with horseradish peroxidase. The amount of bound peroxidase is proportional to the concentration of the ferritin present in the sample. The unbound conjugate is washed off with water. Upon the addition of the chromogen and substrate, the intensity of colour development is proportional to the amount of ferritin in the samples, and is measured by using 450nm microtiter plate reader. The ferritin concentrations of samples are obtained by reference to the standards.

The standard curve is obtained by plotting the absorbance (Y-axis) versus the corresponding concentration of standards (X-axis). The ferritin concentrations of samples, which are run concurrently with the standards, can be determined from the standard curve.

MATERIALS PROVIDED

1. Microwell Stripes: Anti-Ferritin antibodies coated wells, 96 wells.
2. Enzyme Conjugate (11 mL): Anti-Ferritin Ab conjugated to horseradish peroxidase.

3. Sample Diluent or Zero Standard (11 mL): Phosphate buffered saline with protein.
4. Reference Standard Set (0.50 mL/each): Human ferritin standards in the phosphate buffered saline with protein. Five levels of standards are calibrated to 15, 50, 200, 400 and 800 ng/mL against NIBSC 80/602.
5. Solution A (11 mL): Buffer solution containing hydrogen peroxide.
6. Solution B (11 mL): Tetramethylbenzidine.
7. Stop Solution: 2 N HCL.
8. Well holder for securing individual well.

SPECIMEN COLLECTION AND HANDLING

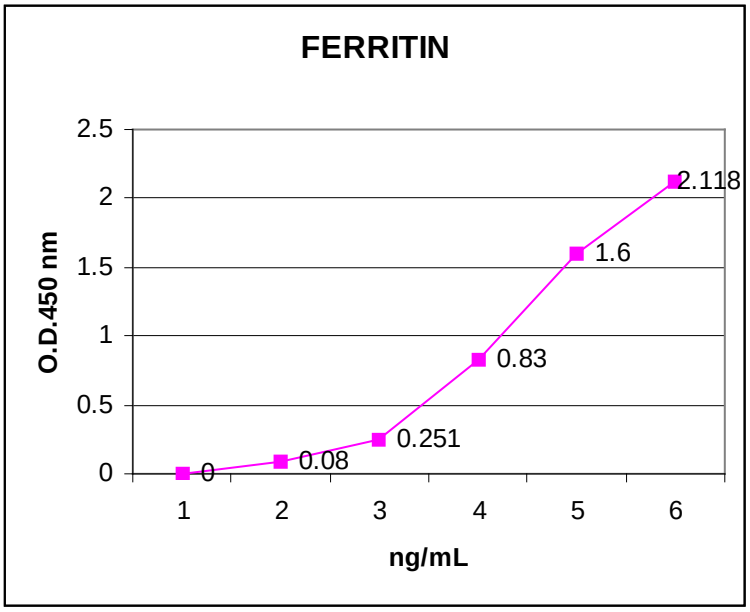
Blood is Collected by venipuncture and allowed to Clot. serum is separated by centrifugation at room temperature. If sera cannot be assayed immediately, they are stored at 2-8^{o}C or frozen.

CALCULATION OF RESULTS

1. Plot the concentration (X) of each Reference Standard against its absorbance (Y) on a full logarithmic graph paper.

2. The ferritin value of patients are obtained by reference to the standard curve as follows:

Well #	Description (ng/mL)	Absorbance (450 nm)	Value from STD Curve
A1 B1	0	0.001 0.003	
A2 B2	15	0.081 0.087	
A3 B3	50	0.243 0.251	
A4 B4	200	0.884 0.830	
A5 B5	400	1.467 1.417	
A6 B6	800	2.068 2.118	
A7 B7	Patient A (Serum)	0.684 0.708	165 ng/mL


FERRITIN
O.D.450 nm
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
ng/mL
0
0.08
0.251
0.83
1.6
2.118

OBSERVATION AND RESULTS

The Normal value of serum ferritin is less than 240 ng/ml and values above 240 is considered as abnormal

DISTRIBUTION OF PATIENTS

		n	%
sex	Male	41	74.5%
	Female	14	25.5%
smoker	No	33	60.0%
	Yes	22	40.0%
ALCOHOLIC	No	41	74.5%
	Yes	14	25.5%
HYPERTENSION	No	34	62%
	Yes	21	38%
diabetes	No	41	74%
	Yes	14	26%
serum ferritin	Normal	36	65.5%
	Abnormal	19	34.5%

		serum ferritin			
		normal		abnormal	
		n	%	n	%
sex	Male	25	69.4%	16	84.2%
	Female	11	30.6%	3	15.8%
smoker	No	20	55.6%	13	68.4%
	Yes	16	44.4%	6	31.6%
ALCOHOLIC	No	30	83.3%	11	57.9%
	Yes	6	16.7%	8	42.1%
HYPERTENS	No	26	61.9%	8	61.5%
ION	Yes	16	38.1%	5	38.5%
diabetes	No	28	75.7%	13	72.2%
	Yes	9	24.3%	5	27.8%

$\chi 2=1.4$ P=0.23 NS

$\chi 2=0.8$ P=0.35 NS

$\chi 2=4.2$ P=0.04 S

$\chi 2= 0.01$ P=0.98 NS

$\chi 2=0.08$ P=0.78 NS

To have a significant value

$\chi 2$ (Chi.Square) value should be more than or equal to 3.84.

The P value should be less than or equal to 0.05

Of the 55 patients 41 were males and 14 females,

22 were smokers (40%)

39% showed high ferritin among nonsmokers while 27% showed high ferritin among smokers

25% are alcoholic in our study

27% showed high ferritin among non-alcoholic while 58% showed high ferritin among alcoholic.

38% are hypertensive and 14% of diabetic in our study

24.3% showed normal ferritin among diabetic while 27.8% showed abnormal ferritin among diabetic

38.1% showed normal ferritin in hypertensive while 38.5% showed abnormal ferritin in hypertensive

40% male and 21% female showed raised serum ferritin level

serum ferritin * glasgow

		glasgow					Total
		1	2	3	4	5	
serum ferritin	Normal	0	2	6	11	17	36
	Abnormal	1	9	8	0	1	19
Total		1	11	14	11	18	55

$\chi 2=28.4$ P=0.001

significant association between level of ferritin and prognosis of patient

		glasgow		Total
		bad	good	
serum ferritin	Normal	8	28	36
	Abnormal	18	1	19
Total		26	29	55

$\chi 2=26.2$ P=0.001

significant association between level of ferritin and prognosis of patient

Group Statistics

	glasgow	N	Mean	Std. Deviation	t-test
SERUM FERRITIN	Bad	26	289.2919	128.72244	t=7.5 P=0.001 Significant
	good	29	88.3441	61.76006	

Mean serum ferritin among patients with bad prognosis is 289.29

Mean serum ferritin among patients with good prognosis is 88.34

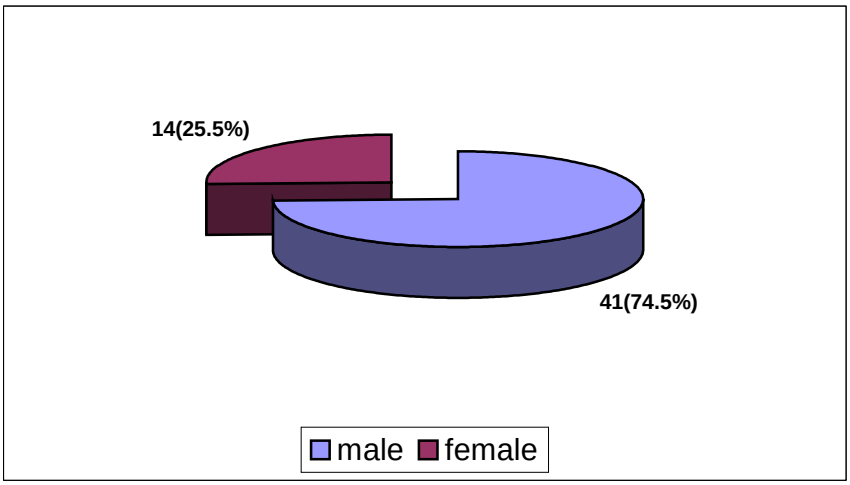
SERUM FERRITIN

	N	Mean	Std. Deviation	ANOVA F-test	Minimum	Maximum
1	1	479.5900	.		479.59	479.59
2	11	321.9036	114.74966		86.00	456.91
3	14	250.0757	128.03815	F=17.3	3.58	425.15
4	11	97.4918	57.00953	P=0.001	20.84	218.78
5	18	82.7539	65.44719		7.89	300.00
Total	55	183.3376	141.06805		3.58	479.59

Correlations

		glasgow
SERUM FERRITIN	Pearson Correlation	-.735(**)
	Sig. (2-tailed)	.000
	N	55

** Correlation is significant at the 0.01 level (2-tailed).



DISCUSSION

Iron is an essential element for the human body. It has, however, been suggested that excessive iron stores may increase the risk of vascular disease.

There are many studies saying Ferritin is risk factor for myocardial infarction. This is because Iron catalyzes the formation of extremely reactive hydroxyl radicals (Fenton reaction). Interaction with lipids may initiate the formation of oxidized LDL that ultimately leads to the development of foam cells and progression of atherosclerosis.[39] Additionally, iron could also play a role in vascular disease by activating platelets via a protein kinase C mechanism.

But recently it is considered that ferritin is also a prognostic factor in stroke. This is due to the damage caused by Iron during Ischemia / Reperfusion[40/41]. During the reperfusion after cerebral infarction, there is a marked increase in oxygen-radical production as well as a release of iron ions, leading to progressive tissue damage and cellular death. Because of its specific areas rich in iron, high amounts of polyunsaturated fatty acid side chains in membrane lipids, and low concentrations of antioxidant enzymes, such as superoxide dismutase, catalase and glutathione peroxidase, the brain may be especially vulnerable to oxidative stress. So iron is considered as an important factor deciding the amount of damage .

In our study the correlation between various factors like smoking ,alcohol , diabetes , hypertension and ferritin are studied .

Similarly the outcome of stroke is correlated with serum ferritin in our study .

Smoking:-

In our study 33 patients are non – smokers and 22 patients are smokers, of which 44% are smokers with normal ferritin and 31.6% are smokers with raised ferritin

The P value is .35 which is non significant. So in our study there is no correlation between ferritin and smoking.

Alcohol:-

41 patients are non – alcoholic and 14 patients are alcoholic in our study, of which 16.7 % are alcoholic with normal ferritin and 42.1 % are alcoholic with raised ferritin.

The P value is .04 and x^2 (chi Square) Value is 4.2 which is significant. So in our study there is definite correlation between alcohol and Serum Ferritin.

Effect of alcohol consumption on indices of iron stores and of iron stores on alcohol intake by WHITFIEND JB; ZHUG; HEALTH AC; POWELL AND LW etal. Showed there is definite correlation between alcohol and Serum Ferritin.

HYPERTENSION:-

34 patients are non- hypertensive and 21 patients are hypertensive in our study of which 16 (38.1%) are hypertensive with normal ferritin and 5 (38.5%) are hypertensive with raised ferritin. The P value is .98 which is non- significant.

"Increased in Serum Ferritin is common in men with essential hypertension (by ANDREW A.SKOLNICK. Says Serum Ferritin level is increased in hypertensive men. But in our study we don't have any correlation.

Diabetes:-

41 patients are non-diabetic and 14 patients are diabetic in our study , of which 9 (24.3%) are diabetic with normal ferritin and 5 (27.8%) are diabetic with raised ferritin.

The P value is .78 which is non – significant.

ALBERT LACUBE, MD,CRISTINA FERNANDES,

MD,JOANGENESCA, MD in their study entitled diabetes is the main factor accounting for the high Ferritin levels detected in Chronic hepatitis C virus infection says that Serum Ferritin level is increased in diabetes. But in our study there is no correlation.

Ferritin and out come:-

In our study 29 patients had good prognosis and 26 patients had bad prognosis. Of the 29 patients with the good prognosis 28 had normal Serum Ferritin and only one had

raised Serum Ferritin. Of the 26 patients with bad prognosis 18 had raised Serum Ferritin and only 8 had normal Serum Ferritin.

This has a P value of .001 and x^2 (Chi. Square) value of 26.2. Which is clearly significant. So our study concludes that raised Serum Ferritin is associated with poor prognosis. There are other studies favoring this fact.

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CONCLUSION

In patients with Acute Ischemic stroke

- Serum ferritin levels can be used as a prognostic indicator
- Antioxidants can be added as a part of treatment protocol in patients with Acute Ischemic stroke.
- Iron restriction should be done in persons with high risk for Ischemic Stroke.
- Serum ferritin measurement should be routinely done in high risk patients like serum glucose and cholesterol measurement.

Drugs like Deferroxamine can be used to reduce serum ferritin levels.

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PROFORMA

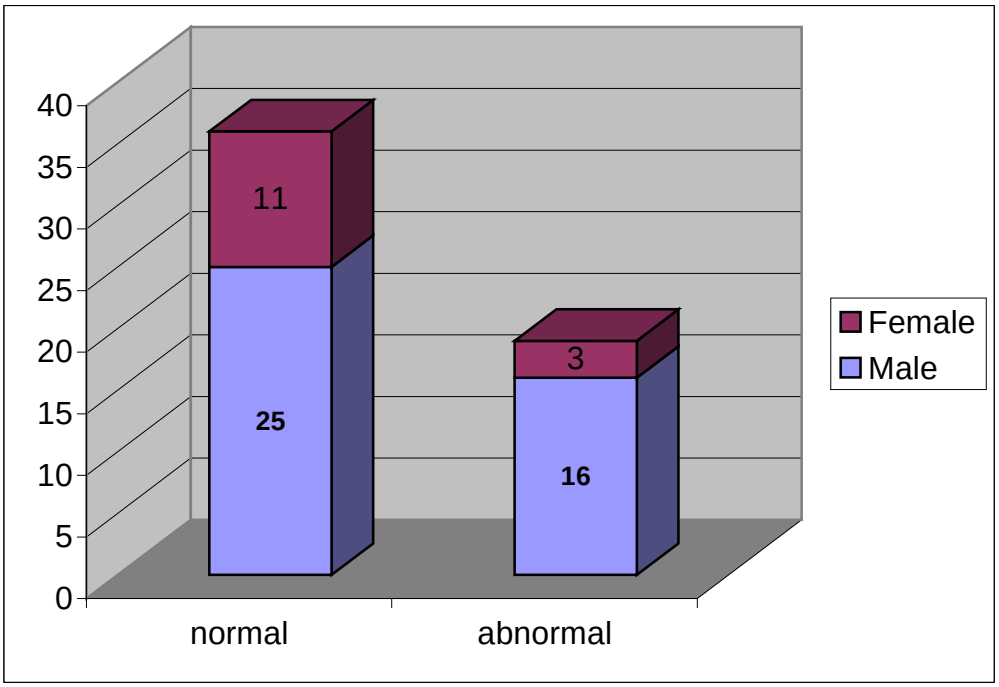
NAME	:	Ward No.	:
SEX	:	Unit	:
I.P.NO.	:	Date of admission	:
Serial No.	:		
Age	:		
Diabetes	:		
Hypertension	:		
Smoking	:		
Alcohol	:		
Blood ESR	:		
Blood CRP	:		
Time of Blood sample			
after stroke onset	:		
C.T. Scan Brain	:		
Serum Ferritin	:	GOS:	

MASTER CHART

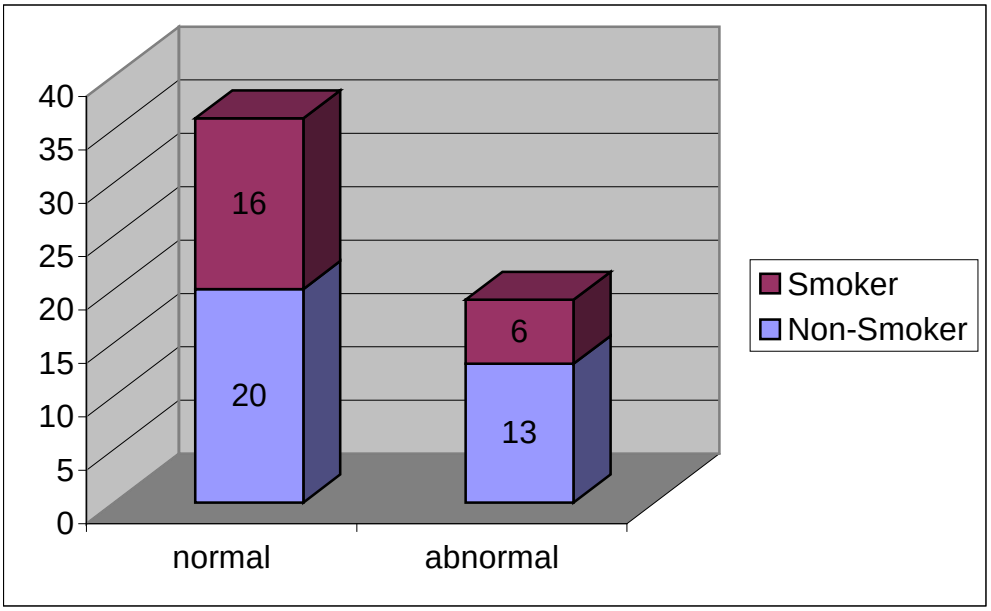
S no	Name	Age in yrs	Sex	Time of sample collection from the episode in hrs	Smoker	Alcoholic	Hypertension	Diabetes	Glasgow outcome scale	Serum ferritin
1	SELVARAJ	45	M	8	√		√		3	244.44
2	RAMAN	86	M	8	√		√		3	244.44
3	VENKATESAN	30	M	10	√				5	85.63
4	NATARAJAN	65	M	8					2	456.91
5	ANGAMMAL	75	F	10					5	132.73
6	ANNAMMAL	65	F	12				√	3	224.44
7	MUTHU KRISHNAN	75	M	12	√		√	√	2	184.14
8	JANAKI AMMAL	57	F	12			√	√	4	32.11
9	SELVI	35	F	10			√		5	80
10	AMEENA BEEVE	65	F	10			√		4	96.64
11	MANIKANDAN	60	M	12					1	479.59
12	KANNAN	70	M	10					5	42.61
13	IRSAMMAL	70	F	14			√		4	122.45
14	GOVINDAN	15	M	14					3	425.15
15	MUNU SAMI	75	M	20				√	3	137.66
16	ELLAMMAL	40	F	16				√	4	118.61
17	KASTHURI	60	F	16			√	√	5	29.19
18	THABITHAMMAL	70	F	12			√		5	7.89
19	RAMALINGAM	57	M	14	√	√			5	47.47
20	ROSE	60	M	18	√	√			4	93.36
21	SUBRAMANIYAN	75	M	22	√	√			4	20.84
22	SAMBANTHAM	76	M	18	√				4	145.16
23	ARUMUGAM	65	M	12	√				3	188.85
24	JALAPUSHPAM	55	M	12					3	376.83
25	ABDUL RAHIM	75	M	14					2	86

26	LAKSHMI	55	F	6					4	218.78
27	AHIMA BEEVI	55	F	8					2	258.54
28	SHEIKH IBRAHIM	56	M	4	√	√	√	√	2	443.59
29	GURU SAMI	65	M	8	√	√	√	√	5	300
30	ARUMUGAM	60	M	4					5	74.43
31	HOWDHA	57	M	10	√				2	296.83
32	NAGARAJ	52	M	8					5	168.71
33	SABAPATHY	54	M	10					4	114.5
34	SAMUEL	60	M	10		√			2	345.64
35	SUDALAI MANI	42	M	4					2	328.72
36	RANGANADHAN	55	M	10					3	3.58
37	GANESH	50	M	4					3	381.48
38	JOHN	62	M	14		√			2	415.38
39	RAJASEKAR	52	M	6	√	√			3	314.39
40	LAKSHMI AMMAL	55	F	10		√	√	√	3	412.91
41	MAHESHWARI	62	F	4				√	2	420.51
42	RAMALINGAM	63	M	10			√	√	4	68.71
43	RAMAN	52	M	4		√	√		5	59
44	ANTONY	60	M	18	√		√		5	53.43
45	PUSHPARAJ	65	M	4	√				4	41.25
46	GANESH	53	M	12	√		√		5	85.79
47	RAVI	61	M	10	√		√		5	71.43
48	KUMARA SAMI	35	M	4		√			3	276
49	RAMESH	31	M	10	√				3	52.79
50	KRISHNAMURTHY	52	M	10	√		√		3	218.1
51	MARIMUTHU	63	M	10		√			2	304.68
52	MURUGAN	65	M	10	√	√	√		5	71.43
53	PRIYA	72	F	10				√	5	85.79
54	RAMESH	64	M	8	√	√	√	√	5	41.25
55	RAVI	60	M	10	√		√	√	5	52.79

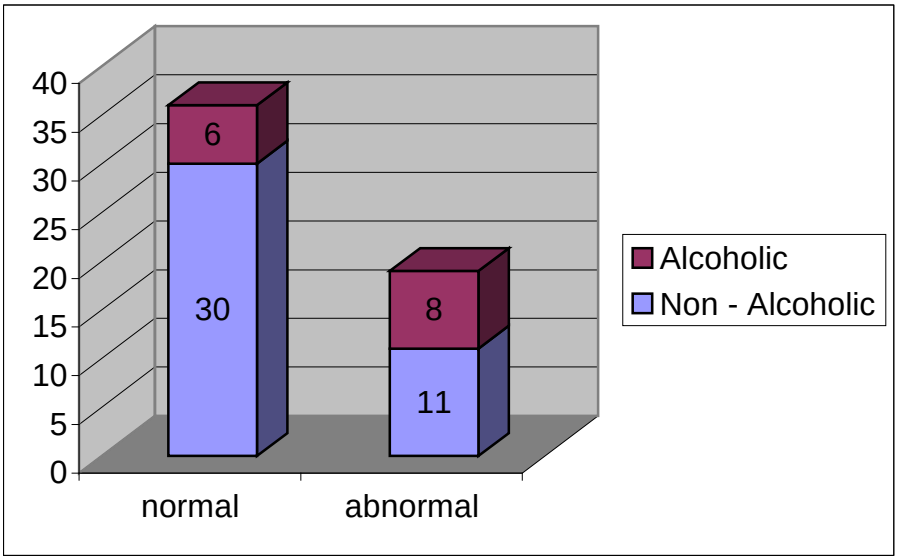
SEX AND FERRITIN



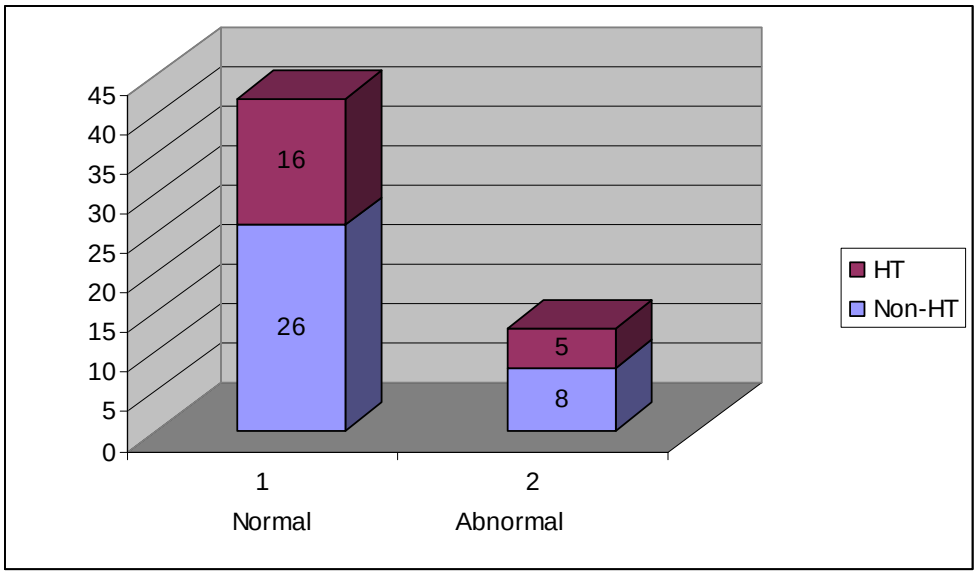
SMOKING AND FERRITIN



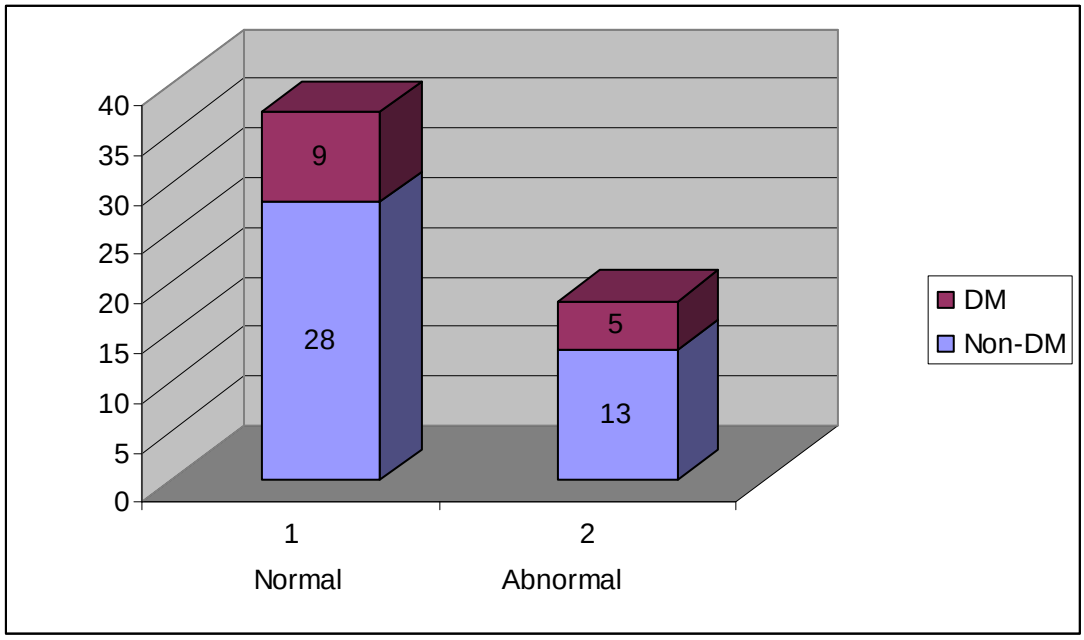
ALCOHOL AND FERRITIN



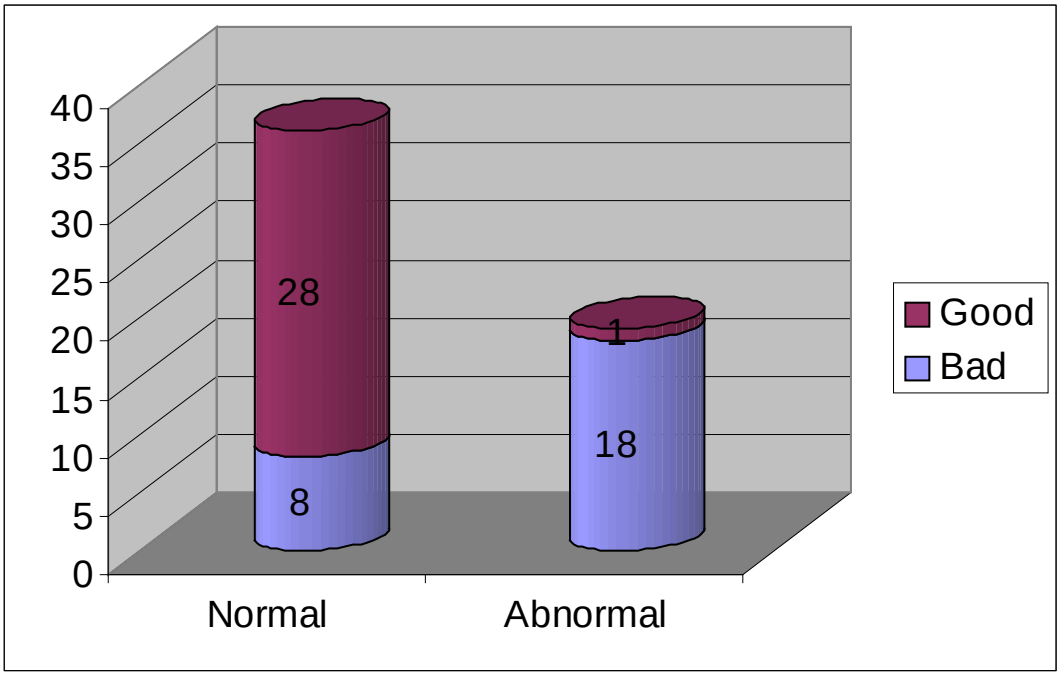
HYPERTENSION AND FERRITIN



DIABETES AND FERRITIN



FERRITIN AND OUTCOME



MEAN FERRITIN AND PROGNOSIS